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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,164	11/09/1999	BENJAMIN EITHAN REUBINOFF	13164	6220

7590

05/22/2002

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EXAMINER

WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 05/22/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/436,164

Applicant(s)

REUBINOFF ET AL.

Examiner

Joseph Woitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 March 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 and 29-46 is/are pending in the application.
- 4a) Of the above claim(s) 1-18, 29-36, 45 and 46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-26 and 37-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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DETAILED ACTION

This application is an original application filed November 9, 1999 which claims benefit of foreign applications PP7009, filed November 9, 1998, and PQ2852, filed September 15, 1999, both filed in Australia.

Applicants' amendment filed March 4, 2002, paper number 14 has been received and entered. The specification has been amended. Claims 27 and 28 have been canceled. Claims 19, 20 and 22-26 have been added. Claims 37-46 have been added. Claims 1-26 and 29-46 are pending. Newly added claims 45 and 46 encompass a method for preventing and treating a disease and are properly restricted to group VII. Therefore, claims 1-18, 29-36, 45 and 46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10. Claims 19-26 and 37-44 are currently under examination.

This application contains claims drawn to an invention non-elected with traverse in Paper No. 10. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

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Claim Objections

Claims 19-28 objected to because of informalities is withdrawn. Amendments to the claims have obviated the basis of the objection.

Specification

The objection to the abstract is withdrawn. Amendments to the abstract and to the specification indicating SEQ ID NOs have obviated the basis of the objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-26 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of culturing a human pluripotent embryonic stem cell and deriving spontaneously differentiated cell types therefrom, does not reasonably provide enablement for culturing human totipotent embryonic stem cells or methods for the controlled differentiation of a stem cell is withdrawn.

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First, Applicants point out that claims have been amended to encompass 'pluripotent stem cells' in an effort to favorably advance the prosecution of the present application. With regard to the ability to controllably or spontaneously differentiate a cell Applicants point out that the claims are expressly directed to inducing differentness and argue that though the specification does not specifically exemplify each and every aspect of the claimed invention, Applicants are not required to provide working examples, citing *In re Anderson*, and that one enabled embodiment could be extrapolated to other embodiments by the skilled artisan, citing *In re Wright*. See Applicants' amendment, pages 9-10. Applicants' arguments have been fully considered.

Amendment to the claims to encompass 'pluripotent' stem cells has obviated this portion of the rejection. With respect to the ability to controllably or spontaneously differentiate a cell Examiner agrees that working examples need not be provided. As noted by Applicants, the instant disclosure does not provide a working example for the controlled differentiation of a cell, additionally it is noted the specification does not provide any specific methodology or reference to teachings for controllably obtaining a differentiated cell. Therefore, the instant specification would be restricted to methods that are generally known in the art for obtaining a differentiated cell. A review of the art of record indicates that the skilled artisan has been capable of preferentially differentiating pluripotent cells with the addition of particular growth/differentiating factors (see for example Thompson *et al.* IDS reference AG or Martin IDS reference AE). Examiner agrees that one of skill in the art can extrapolate the use of methods

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known in the art for differentiation of a pluripotent cells. It is noted that the specification does not teach that the pluripotent human stem cells are different from pluripotent stem cells previously disclosed in the art. Further, the specification does not disclose specific teaching for methodology for the controlled differentiation of human cells and thus, relies on the art to practice the method in the full breadth of the claim. Upon review of the art of record and the instant specification, Examiner can not find any specific support for why methods known in the art for differentiating a pluripotent cell could not reasonably be extended for use in the method as instantly claimed. It is noted that the art does not teach or support enablement of methodology for the controlled differentiation of all the possible somatic cell types, however the instant claims do not specifically recite these non-enabled embodiments.

Therefore, for the reasons above, the rejection is withdrawn.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-26 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Amendments to the claims and Applicants' arguments have obviated the basis of each of the specific rejections.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 19-26 stand rejected and claims 37-44 are newly rejected under 35 U.S.C. 102(b) as being anticipated by Thomson *et al.* (Science 282:1145-1147).

Applicants summarize the basis of the rejection and point out that the instant methods are drawn to a method practiced *in vitro*. Applicants argue that Thomson *et al.* do not teach *in vitro* methods, rather *in vivo* culturing methods. See Applicants amendment, middle of page 13. Applicants' arguments have been fully considered but not found persuasive.

Examiner notes that amended claims 19-26 are drawn to a method for culturing and differentiating human undifferentiated embryonic stem cells *in vitro*. Further, Examiner agrees that Thomson *et al.* teaches methods for the *in vivo* culturing and differentiation of embryonic stem cells (for example page 1146; middle of first column and page 1147; figure 4). However, as noted in the previous office action, in characterizing the cell lines, various culturing methods were used to differentiate the cell lines. Among the parameters taught to affect differentiation of

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the cell lines was the presence and absence of a feeder layer, the cell density, and various growth factors (see for example page 1146, middle of first column). Thomson *et al.* teach that the lines in culture, differentiation of the cells results in various cell types (Figure 4B and page 12, middle of first column) and point to the references in the prior art which support more detailed methods for differentiation (page 1147; bottom of first column and in reference to citations 22-24). In view of the breadth and generality of the claimed methodology in claims 19-26, the methods and general teachings of Thomson *et al.* describing methods to stimulate or allowing the cell lines to differentiate in culture, anticipate the methods of claims 19-26 and 37-44.

Therefore, for the reasons above and of record, the rejection is maintained.

Claims 19-26 stand rejected and claims 37-44 are newly rejected under 35 U.S.C. 102(e) as being anticipated by Thomson (US Patent 6,200,806).

Applicants note that Thomson teaches differentiation of ES cells into extraembryonic cells, pointing to col. 15 lines 10-26 and 50-57. Applicants argue that nowhere does the patent teach the differentiation into cells of the extraembryonic lineage. See Applicants amendment, bottom of page 13. Applicants' arguments have been fully considered but not found persuasive.

Upon review of the portions of the disclosure pointed to by Applicants, Examiner would agree that a unique feature of some of the cell lines disclosed by Thomson is their ability to differentiate into extraembryonic tissue as compared to mouse ES cells. However, it is noted that these cell lines are capable of differentiating into other cell types besides those present in an

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extraembryonic lineage. For example, in column 18, lines 1-43, Thomson teaches that when cultured in high density, ES cells are capable of differentiating into multiple lineages. Further, the conditions to culture the cells in gelatin treated culture plates and allowed to grow for two weeks after achieving confluence, or when cells are grown without a fibroblast feeder layer the ES cells spontaneously differentiate (description in paragraphs bridging columns 14-15 and in Figure 6). Throughout the disclosure of Thomson the growth factors and conditions necessary for the proliferation and differentiation of the specific ES cell lines are described. Additionally, Thomson notes that while the mechanisms controlling the differentiation of ES cells are not known, it may be possible to differentiate the ES cells to specific cell types *in vitro* (column 16; lines 45-56). Given the breadth of the instant claims, and in light of the nature and similarity of the instant disclosure and that of Thomson for the culturing and differentiation of ES cells, the instantly claimed methods are anticipated.

Therefore, for the reasons above and of record, the rejection is maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Deborah Crouch
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